

Gastrointestinal stromal tumor: Retrospective evaluation of twenty cases

Gastrointestinal stromal tumor

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Abstract

Aim: In this study, we aimed to evaluate the clinico-pathological findings and treatment methods of 20 cases operated for intra-abdominal gastrointestinal stromal tumor.

Material and Methods: The data of 20 cases operated at Erzurum Regional Education and Research Hospital, Erzurum, Turkey between 2015 to 2020 were retrospectively analyzed. Gastrointestinal stromal tumor (GIST) locations, surgical methods, histopathological diagnosis, postoperative medical treatments were discussed.

Results: Eleven (55%) patients were male, and nine (45%) were female, and the mean age of all patients was 57.7 ± 11.42 (39-76) years. Most of the tumor was in the stomach (70%). Abdominal pain and bleeding were the main symptoms at admission. The mean diameter of the tumors was 61.5 ± 30.3 mm (10-120 mm). The most common surgical technique was laparoscopic gastric wedge resection in 7 patients (35%). Seven patients were classified as high risk, 6 as medium risk, 5 as low risk and 2 patients as a very low risk on pathological evaluation. CD117 expression was positive in all patients, and CD34 expression was found to be positive in 15 (75%) patients.

Discussion: Gastrointestinal stromal tumors are mainly located intraabdominally. The most common symptoms are abdominal pain and bleeding. Symptoms depend on the location of the tumor in the abdomen. The main purpose of surgery is the complete resection of the mass performed with a negative surgical margin. Minimally invasive methods can be applied safely in GISTs.

Keywords

Gastrointestinal stromal tumor; Histopathology; Surgical treatment; Minimal invasive surgery

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Introduction

Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor of the gastrointestinal tract [1]. Studies show that the incidence of the GIST is 10 to 15 cases per million. In GIST, a significant relationship between incidence and geographical distribution, race and gender could not be shown [2]. It can be seen that after the 2000s, there has been an increase in the incidence of GIST. This has been reported to be a result of improvement criteria rather than a true incidence increase [3].

GISTs can occur anywhere in the gastrointestinal tract from the esophagus to the anus. More than 90% of GISTs are from the gastrointestinal system (GIS), most often (%51) from the stomach, followed by the small intestine (%36), colon (%7), rectum (%5) and esophagus (%1) rarely mesentery, peritoneum, omentum and also it is seen rarely in the intra-abdominal organs such as liver, pancreas, ovary and uterus [4]. The most common metastasis sites of GISTs are liver and abdominal membranes, peritoneum, mesentery and omentum [5].

Inside and around the myenteric plexus of the intestine, there are pacemaker interstitial Cajal cells responsible for primary gastrointestinal system peristalsis. GISTs are thought to be mesenchymal tumors arising from the precursors of Cajal cells. Cajal cells contain c-kit gene protein that regulates intracellular events. The immune marker of c-kit is CD 117. A mutation in the c-kit proto-oncogene is involved in the pathogenesis of GISTs. As a result, cell growth is stimulated and/or apoptosis is inhibited [6].

The first step in the treatment of GISTs is surgical complete resection. Surgery is potentially curative for primary GISTs that do not metastasize. The probability of recurrence will depend on the malignant potential risk classification criteria. Tumors

are resistant to traditional chemotherapy. In 2002, the first tyrosine kinase inhibitor was used to treat metastatic disease. It is currently used successfully as an adjuvant or neoadjuvant [7]. In this study, we aimed to contribute to the literature by presenting symptoms, diagnostic methods, surgical methods and pathological findings of patients operated for gastrointestinal stromal tumors in our clinic.

Material and Methods

The files of 20 patients who were operated with a diagnosis of GIST at the Department of Gastrointestinal Surgery, Erzurum Regional Education and Research Hospital, Erzurum, Turkey between 2015 and 2020 were retrospectively analyzed after ethical approval (Ethics Committee Decision Number: 2020/12-125).

Demographic data, clinical findings, imaging tools, treatment modalities of the cases were recorded. From the operation notes, the location of the tumor, surgery type, tumor diameter, the presence of invasion into the surrounding tissues, and the status of metastases were evaluated. Tumor diameter and mitosis rate were determined in the histopathological examination of the tumor. CD-117, CD-34, SMA, S-100, Desmin, Vimentin, DOG-1 stainings were performed immunohistochemically. Tumors were categorized as very low, low, medium and high risk according to their potential for malignancy. Adjuvant or neoadjuvant treatment protocols of the cases were recorded. The survival status of the patients was checked by phone call.

Results

A total of 20 patients were included in the study. The mean age of the patients was 57.7 ± 11.42 (39-76) years, 11 of them were men (55%), 9 were women (45%). The most common admission symptoms were abdominal pain and bleeding, while

Table 1. Preoperative and peroperative features of the patients operated for gastrointestinal stromal tumor

Patient No	Age (year)	Gender	Complaints	Diagnostic Tool	Location	Treatment
1	56	M	Incidental	CT and PET	Duodenum	Whipple
2	70	M	AP&GIB	CT and EUS	Stomach	TG
3	52	F	Incidental (Trauma)	Emergency surgery	Jejunum	SR
4	51	M	WL&Swallow difficulty	CT and PET	Jejunum	SR
5	45	M	AP	CT and PET	Jejunum	SR
6	46	M	Vomiting&Nausea	CT and PET	Ileum	SR+RHC
7	76	M	AP&WL&Loss of apatite	CT and EUS	Stomach	PG
8	51	F	AP	CT and EUS	Stomach	OWR
9	68	F	AP&Loss of appetite	CT and EUS	Stomach	LWR
10	67	M	GIB	CT and EUS	Stomach	LWR
11	61	M	AP&Loss of appetite	CT and EUS	Stomach	LWR
12	48	F	AP&GIB&Anemia	CT and EUS	Stomach	LWR
13	74	M	Asymptomatic	CT and EUS	Stomach	LWR
14	66	F	AP&WL&Loss of appetite	CT and EUS	Stomach	LWR
15	57	F	AP	CT and EUS	Stomach	RSTG
16	39	F	GIB	CT and EUS	Stomach	RSTG
17	49	M	AP&Rapid satiety	CT and EUS	Stomach	TG
18	41	F	Incidental	CT and EUS	Stomach	RSTG
19	69	F	Incidental	CT and EUS	Stomach	OWR
20	68	M	Incidental	CT and PET	Jejunum	LSR

AP: Abdominal pain, GIB: Gastrointestinal bleeding, WL:Weight loss, CT: Computed tomography, PET: Positron emission tomography, EUS: Endoscopic ultrasonography, TG: Total gastrectomy, SR: Segmental resection, RHC: Right hemicolectomy, PG: Proximal gastrectomy, OWR: Open wedge resection, LWR: Laparoscopic wedge resection, RSTG: Robotic subtotal gastrectomy, LSR: Laparoscopic segmental resection.

Table 2. Postoperative features of the patients operated for gastrointestinal stromal tumor

Patient No	Tumor diameter (mm)	Risk category	CD117	CD34	Desmin	SMA	S100	DOG-1	LOS (days)	Outcomes	Follow-up (months)
1	40	Low	+	+	-	+	NS	NS	16	SSI	38
2	35	Low	+	+	-	+	-	+	9	-	61
3	40	Low	+	+	-	+	NS	+	8	Exitus (Cranial trauma)	0
4	80	Medium	+	-	NS	NS	-	+	7	-	33
5	120	High	+	+	NS	NS	NS	NS	9	-	24
6	90	Medium	+	+	-	+	-	+	12	Ileus	16
7	50	Very low	+	+	-	NS	-	NS	9	-	18
8	55	High	+	+	-	-	-	+	6	-	24
9	110	High	+	-	-	-	-	NS	9	Atelectasis	28
10	30	Medium	+	+	NS	NS	NS	NS	8	-	39
11	95	Low	+	+	-	NS	-	NS	7	-	58
12	70	High	+	+	-	-	+	+	10	Port side infection	60
13	15	Medium	+	+	-	-	-	+	6	-	22
14	85	Medium	+	+	NS	NS	NS	NS	7	-	29
15	45	Medium	+	-	-	NS	-	+	8	-	54
16	90	High	+	-	-	-	-	NS	12	Port Side infection	52
17	60	High	+	-	-	+	-	NS	11	Atelectasis	38
18	50	Low	+	+	-	-	-	-	4	-	39
19	60	High	+	+	-	-	-	NS	6	-	47
20	10	Very low	+	+	+	-	-	+	7	-	59

NS: Not studied, SSI: Surgical site infection.

other rare symptoms were weight loss, anorexia, dysphagia and rapid satiety. Half of all patients had abdominal pain, and 4 (20%) patients had gastrointestinal bleeding. Massive bleeding was not observed in any of our GIST cases. All bleeding cases were applied with the complaint of melena not required erythrocyte suspension. None of the patients had tumor marker elevation. Contrast-enhanced abdominal tomography was performed in all cases preoperatively, except for the case of GIST, which was incidentally detected due to trauma. Endoscopic ultrasonography was performed to confirm the diagnosis in all stomach localized GISTs. PET was used in extra-gastric GIST patients. MRI was not used in any patient at the time of diagnosis. At the preoperative evaluation, only one patient had distance metastasis (liver metastasis). This patient was operated after 12 months of neoadjuvant tyrosine kinase inhibitor therapy.

All patients were operated with general anesthesia. While only one patient was operated under emergency conditions due to trauma, the other patients were operated under elective conditions. It was seen that 14 (70%) of all cases originated from the stomach, 4 from the jejunum, one from the duodenum, and one from the ileum. The mean diameter of the tumors was 61.5 ± 30.3 mm (10-120 mm). In the intraoperative evaluation of a patient who operated under emergency condition, incidentally, jejunum located GIST was seen and the mass was resected. In addition, half of all patients were operated with minimally invasive surgery (laparoscopic or robotic). Laparoscopic gastric wedge resection was performed in 6 of 14 gastric GIST patients, and 3 of 14 gastric GIST patients underwent robotic subtotal gastrectomy. One patient with jejunum located GIST was operated with laparoscopic segmental resection. All of the

patients who started their surgery with a minimally invasive method were completed with the same method. Preoperative and peroperative features of the patients are seen in Table 1.

Two (10%) patients were at very low risk, 5 (25%) patients were at low risk, 6 (30%) were at medium risk, and 7(35%) were at high risk in pathological evaluation. A spindle cell pattern was seen in 16 patients (80%), epithelioid pattern in 2 patients (10%), and a mix pattern in 2 patients (10%). CD 117 was 100 % positive, CD 34 was 75% positive. DOG-1 positivity was seen in 9 of 10 patients. SMA was positive in 5 of 13 patients. Desmin-positivity was seen in only one patient (1/19). S100 was positive in 1 of 15 patients. The postoperative features of the patients are presented in Table 2.

The mean length of hospital stay was 8.55 ± 2.7 days (4-16). The morbidity and mortality rates of the study were 30% and 5%, respectively. The most common complication was surgical site infection with 15% (2 of 3 at port side, and 1 of 3 at abdominal incision). A patient who died due to cranial trauma on postoperative day 8 was incidentally detected to have Jejunum localized GIST. The mean postoperative follow-up time was 36.95 ± 17.08 months (0-61). No patient died, except for the patient who died in the early postoperative period.

Discussion

The gastrointestinal system is a long path that continues with each other from mouth to anus. The most common type of cancer in this system is adenocarcinoma [8]. The second most common type is squamous cell cancer. Apart from the common types, gastrointestinal stromal tumor (GIST), lymphoma, carcinoid tumor and leiomyosarcoma are other types of gastrointestinal system tumors. In this study, it was aimed to evaluate GIST

cases, which are rare in the gastrointestinal tract, together with our surgical experience.

GIST is of mesenchymal origin and constitutes approximately 80% of all gastrointestinal mesenchymal tumors [9]. Although GISTs are rarely seen in the pediatric age group, the average age at which they are most common is 60 years, and they have an almost equal distribution in female and male populations [2]. In our study, the mean age was 57.7 ± 11.42 (39-76) years, and the male to female ratio was 1.2 (11 male, 9 female), compatible with the literature.

GIST is mostly asymptomatic at an early stage and is detected incidentally during surgical interventional, radiological examination, or endoscopy performed for another reason. In symptomatic GIST, symptoms are not specific to GIST, but they cause complaints according to the location and the size of the tumor. The most common symptoms are abdominal pain (50-70%), gastrointestinal bleeding (20-30%) and abdominal mass (5-10%) as well as nausea, vomiting, dysphagia, weight loss, bloating, perforation and obstruction [9]. In our study, the most common symptoms were abdominal pain and gastrointestinal bleeding. GISTs often grow towards the abdominal cavity and become large masses in the abdomen, signs of intestinal obstruction are relatively rare. In our study, only one case had obstruction findings. This case was located at the terminal ileum and was treated with segmental resection and right hemicolectomy.

Although CT is the most common radiological method used for the diagnosis of GIST, endoscopic ultrasonography, magnetic resonance imaging and positron emission tomography are used as auxiliary tests. However, no radiological examination is sufficient to make a definitive diagnosis of GIST [10]. Abdominal CT with dynamic triphasic contrast, EUS and PET were performed on all our patients in the preoperative period as an imaging tool. No patient underwent MRI in the preoperative period.

Biopsy and evaluation with immunohistochemistry are required for the definitive diagnosis of GIST. Preoperative routine fine-needle aspiration biopsy is not recommended for GIST suspicious masses. Since it carries the risk of disruption of the capsule integrity of the tumor and implantation of tumor cells. A preoperative biopsy is necessary only for neoadjuvant treatment in cases with suspected GIST that cannot be surgically removed or is considered to be a risky surgery [11].

In the GIST, tumor size, mitotic rate, patient age and tumor localization are considered as independent prognostic factors [12]. Tumor rupture and the presence of metastasis at the time of diagnosis have a significant negative effect on the disease-free period and are associated with a poor prognosis [13]. It is thought that the invasion of the surrounding tissue of the tumor and the advanced age of the patient are effective in the aggressiveness of the tumor [12]. It has been reported that small intestinal GISTs with the same size and mitosis ratio have a worse course than gastric GISTs. It is accepted that the location with the best overall survival is the esophagus, and the small intestine is the worst [14]. In our series, there were only stomach and small intestine GISTs.

Since GISTs have a very low tendency to lymphogenous metastasis, routine lymph node dissection is not required

during surgical treatment [15]. Since there are not many infiltrative tumors, a clean border can be obtained easily. The standard treatment in GIST is surgical complete resection. It is important to remove the tumor with a clean surgical margin without perforating it [16]. Partial resection of the stomach or segmental resection of the intestine is usually sufficient for treatment. Since it is possible to achieve surgical principles for GISTs with minimally invasive methods, laparoscopic resections are widely applied, especially for gastric GIST. Clean surgical margins were obtained in all of our patients who were operated in our series.

All GISTs are considered to have malignancy potential. Fletcher et al. used the maximum tumor diameter and mitosis (50 BBAs) in 2002 to determine the malignancy potentials of GISTs. They divided GIST into four groups as very low risk, low risk, medium risk and high risk. Immunohistochemically, GISTs show 95% staining with CD117, 60-80% with CD34 and 30-40% with SMA. Staining with S-100 and desmin is extremely rare [17]. In our study, CD 117 positivity was 100%, DOG-1 positivity 90% and CD 34 positivity 75%. Desmin-positivity was seen only in one patient (1/19), while SMA was positive in 5 of 13 and S100 in 1 of 15 patients.

Synchronous monitoring of a GIST with another malignant tumor is reported to be between 4.5-35% in the literature. Gastrointestinal adenocarcinoma, prostatic adenocarcinoma, lymphoma, leukemia and breast cancer are the most common GIST-related cancers [18]. Most of the associations of gastrointestinal adenocarcinoma and GIST have been presented as case reports only. In our study, GIST was detected incidentally in 3 cases in a patient who underwent Whipple for pancreatic head tumor, in the third part of the duodenum, in the jejunum in a case operated for gastric adenocarcinoma, and in a case in the stomach corpus.

There may be lymphatic metastases of GISTs at a rate of 0-3.4%. It can also metastasize to the liver, lungs and bones by a hematogenous route [19]. About 15-30% of patients with GIST have metastases at the time of diagnosis. Distant metastases are most common in the liver (50-60%) and peritoneum (20-40%). Although GISTs of ≤ 2 cm have been reported to be metastatic with a low frequency (but not 0%) [20]. The spread to the lungs and bone is very low. Rectal GIST especially often metastasizes to the lungs [21]. Only one of our patients had liver metastasis.

A neoadjuvant tyrosine kinase inhibitor is the standard treatment for patients with unresectable locally advanced tumor, recurrence, and widespread metastasis, a general condition unsuitable for surgery and a positive for c-kit receptor [22]. In addition, preoperative tyrosine kinase inhibitors effectively reduce the size of the tumor and allow organ-preserving surgery in specific locations such as the stomach, cardia, duodenum, and rectum. The optimal duration of preoperative imatinib use should be determined jointly by multidisciplinary team members following the response to treatment. Patients who are initially unsuitable for surgical treatment should be reevaluated for surgery within 1 year after tyrosine kinase inhibitor therapy and surgical treatment should be recommended to patients who are eligible for surgery. Postoperative tyrosine kinase inhibitors significantly prolong both progression-free survival and overall

survival of patients [4]. On the preoperative evaluation, only one patient had liver metastasis. This patient was operated after 12 months of neoadjuvant tyrosine kinase inhibitor therapy.

Previous studies have reported that the overall and grade III–V complication rates were 9–58% and 0–18%, respectively (23, 24). On the other hand, according to data from the USA, the 5-year GIST-specific mortality rate was 12.9% [20]. In our study, the overall complication rate was 30%, which was suitable with the literature, and the overall mortality was 5%, which was lower than in the literature. In our study, the mortality rate was lower than in the literature, as patients were followed up only for the first 30 days after surgery.

Conclusion

The most common location of GIST is the stomach. Resection with a negative surgical margin is the basic curative procedure in primary and non-metastatic tumors. Minimally invasive methods can be applied safely. Neoadjuvant and adjuvant protocols should be evaluated and decided by a multidisciplinary team, considering the diameter of the tumor, age of the patient, general condition, location of the tumor and prognostic factors.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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